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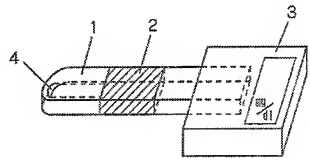
ＱＲ68 ＱＲ82 ＱＳ28 ＱＳ36 ＱＳ39
ＱＸ01 ＱＸ02 ＱＸ04

(54)【発明の名称】　唾液用バイオセンサ

(57)【要約】
【課題】　生体中の特定成分を精度良く測定するためには、血液が必要であり、痛みを伴う測定しかできなかった。
【解決手段】　唾液導入部、少なくとも測定極と対極とからなる電極系、酵素と電子受容体からなる唾液反応部および反応を測定する検知部からなる唾液用バイオセンサを作製し、唾液中の糖濃度を測定することにより、無痛で短時間に簡易に血糖値に相関した糖濃度が測定できる。



Espacenet

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BIOSENSOR FOR SALIVA

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Inventor(s):	KAWAGURI MARIKO +
Applicant(s):	MATSUSHITA ELECTRIC IND CO LTD +
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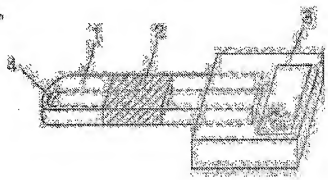
Abstract of JP 2002122562 (A)

PROBLEM TO BE SOLVED: To solve the problem that blood is required in order to determine a specific component in a living body with satisfactory accuracy and that the blood can be determined only by being accompanied by a pain. SOLUTION: The biosensor for saliva is manufactured in such a way that it is composed of a saliva introduction part, an electrode system composed of at least a determination electrode and a counter electrode, a saliva reaction part composed of an enzyme and an electron acceptor and a detection part which measures a reaction. A sugar concentration in the saliva is determined. Therefore, the sugar concentration which is related to a blood sugar value can be determined painlessly, in s short time and simply.



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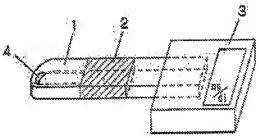
(54) BIOSENSOR FOR SALIVA

(57)Abstract:
PROBLEM TO BE SOLVED: To solve the problem that blood is required in order to determine a specific component in a living body with satisfactory accuracy and that the blood can be determined only by being accompanied by a pain.
SOLUTION: The biosensor for saliva is manufactured in such a way that it is composed of a saliva introduction part, an electrode system composed of at least a determination electrode and a counter electrode, a saliva reaction part composed of an enzyme and an electron acceptor and a detection part which measures a reaction. A sugar concentration in the saliva is determined. Therefore, the sugar concentration which is related to a blood sugar value can be determined painlessly, in a short time and simply.



CLAIMS

[Claim(s)]
[Claim 1]A biosensor for saliva possessing a detection part which measures a saliva reaction part and a reaction which consist of saliva induction, an electrode system which consists of a measurement pole and a counter electrode at least, an enzyme, and an electron acceptor.
[Claim 2]It is the method of measuring a specific component in saliva using a detection part which measures a saliva reaction part and a reaction which consist of saliva induction, an electrode system which consists of a measurement pole and a counter electrode at least, an enzyme, and an electron acceptor, A measuring method of a specific component in saliva measuring change after an enzyme reaction which occurred by saliva supply by said electrode system.
[Claim 3]A biosensor for saliva possessing a detection part which measures a saliva reaction part and a reaction which consist of saliva induction, a saliva supply detection part, an electrode system that consists of a measurement pole and a counter electrode at least, an enzyme, and an electron acceptor.
[Claim 4]Saliva induction, a saliva supply detection part, an electrode system that consists of a measurement pole and a counter electrode at least, It is the method of measuring a specific component in saliva using a detection part which measures a saliva reaction part and a reaction which consist of an enzyme and an electron acceptor, A measuring method of a specific component in saliva measuring change after an enzyme reaction which placed supply of saliva after-detection fixed time in a saliva supply detection part, and occurred between them by said electrode system.
[Claim 5]A biosensor for saliva possessing an absorbance detection part which measures a saliva reaction part and a reaction which consist of saliva induction, an enzyme, an electron acceptor, and chromogen.
[Claim 6]A measuring method of a specific component in saliva which is the method of measuring a specific component in saliva using an optical detection part which measures a saliva reaction part and a reaction which consist of saliva induction, an enzyme, an electron acceptor, and chromogen, and is characterized by measuring coloring after an enzyme reaction by said optical system by saliva supply.
[Claim 7]A biosensor for saliva possessing saliva induction, a saliva supply detection part, an electrode system that consists of a measurement pole and a counter electrode at least, a saliva reaction part which consists of an enzyme and an electron acceptor, a detection part which measures a reaction, and a measuring finish informing part.
[Claim 8]A biosensor for saliva possessing a holding fixture in the sensor mouth, saliva induction, a saliva supply detection part, an electrode system that consists of a measurement pole and a counter electrode at least, a saliva reaction part which consists of an enzyme and

informing part.
[Claim 9]The biosensor for saliva according to claim 1 saliva induction's carrying out form of a major axis with tubed or a space part, and adding a surface-active agent to a point at least.
[Claim 10]The biosensor for saliva according to claim 1 saliva induction's carrying out form of a major axis with tubed or a space part, and adding a surface-active agent to a point at least.
[Claim 11]The biosensor for saliva according to claim 1 saliva induction's carrying out form of a major axis with tubed or a space part, and adding a water absorbing polymer to a point at least.
[Claim 12]The biosensor for saliva according to claim 1 saliva induction's carrying out form of a major axis with tubed or a space part, and adding a fiber layer to a point at least.
[Claim 13]The biosensor for saliva according to claim 1 saliva induction's carrying out form of a major axis with tubed or a space part, and adding a water absorbing polymer to a point at least.
[Claim 14]A biosensor for saliva possessing a fluorescence degree detection part which measures a saliva reaction part and a reaction which consist of saliva induction, an enzyme, an electron acceptor, and chromogen.
[Claim 15]A measuring method of a specific component in saliva which is the method of measuring a specific component in saliva using a fluorescence degree detection part which measures a saliva reaction part and a reaction which consist of saliva induction, an enzyme, an electron acceptor, and chromogen, and is characterized by measuring fluorescence after an enzyme reaction by said optical system by saliva supply.

[Translation done.]

DETAILED DESCRIPTION

[Detailed Description of the Invention]
[0001]
[Field of the Invention]This invention relates to the sensor which detects specific components, such as sugar concentration in saliva.
[0002]
[Description of the Prior Art]By measuring the specific component in blood or urine with progress of the iatrotechnique came to show the check of health, a sick state, the effect of the therapy, etc. However, since it was inspecting with the machine large-sized in a clinical laboratory and the complicated technique of a hospital conventionally, there was a problem that time and expense started. Now, diabetes mellitus is increasing explosively with aging and high-calorie-izing of a meal, and a sensor which can be measured simply at home is desired.
[0003]
[Problem to be solved by the invention]Although an urine sugar sensor is added to a toilet, the trial in which it checks every day also occurs and it is effective for prevention, since there is much influence by a meal and change is also sharp, there is a problem of applying to accuracy. The blood sugar sensor of a short form is used for those who struck the insulin and have controlled sugar concentration by a medical practitioner's instruction. By poking a fingertip with the needle of accessories, a little blood was taken out, the blood sugar level was measured by the sugar sensor, and the dose of an insulin is determined. For the purpose, there is the necessity of measuring the blood sugar level with sufficient accuracy. However, the skin mourns over the method of making it bleed from a fingertip by poking repeatedly with a pain, or it serves as apparatus it is hard for elderly people (person to whom eyesight fell especially by diabetes mellitus) to treat. Then, a sensor which can be measured with sufficient accuracy by aponia is desired.
[0004]
[Means for solving problem]In order to attain the above-mentioned purpose, in this invention Saliva induction, the electrode system which consists of a measurement pole and a counter electrode at least, The sugar concentration simply correlated with the blood sugar level for a short time by aponia can be measured by producing the biosensor for saliva which consists of a detection part which measures the saliva reaction part and reaction which consist of an enzyme and an electron acceptor, and measuring the sugar concentration in saliva.
[0005]
[Mode for carrying out the invention]The biosensor of this invention is targeting saliva as a biological material. Saliva can be taken out by aponia and its burden to a test subject is small. Then, the biosensor which has the saliva induction 1 was shown in drawing 1 as one working

drawing 2 is thin — tubular 1. Or the induction 1 as for which the saliva feed port 4 is vacant in the form which it is as thin as 2-mm5 mm in width in thickness, and is easy to add to a mouth, Next, voltage is applied to the reaction part 2 and electrode system which comprise an electrode system which consists of the layer and measurement pole, and counter electrode of the enzyme glucose oxidase reacted to glucose in saliva, and electron acceptor potassium ferricyanide. The current value which flows in that case is measured, and it consists of the display 3 converted and displayed on glucose concentration. For the ********** reason, the saliva induction 1 and the reaction part 2 have structure which is inserted in the display 3 one whole measurement. The display 3 comprises a panel etc. which consist of the circuit which impresses voltage to a sensor, the current value measuring circuit through which it flows in that case, the circuit which converts a current value into sugar concentration, the timer which measures reaction time, a liquid crystal which displays sugar concentration, or LED.

[0006]Glucose in saliva reacts to glucose oxidase and potassium ferricyanide, and generates potassium ferrocyanide. Measurement of current 5 seconds after impressing +0.7V pulse voltage on the basis of a counter electrode will acquire the oxidation current according to the concentration of the generated potassium ferrocyanide. When linearity was investigated using the reference solution of glucose, it was obtained to 500 mg/dl. The result that the sugar concentration change in saliva follows the blood sugar level is released. Thereby, if the glucose concentration in saliva can be measured with sufficient accuracy, it can apply also to those who are performing insulin injection for blood sugar level control, and can open from pain of extracting blood.

[0007](Embodiment 1) The measurement pole 6 and the counter electrode 7 were formed in the insulating substrate 1 by screen-stencil (drawing 3). On the electrode, dissolved, respectively, applied 40 mg of potassium ferricyanide to 1 cc of carboxymethyl cellulose (CMC) 1% solution as 10 mg of glucose oxidase, and an electron acceptor, it was made to dry at 80 degrees, and the reaction layer 9 was formed. The substrate 1 used polyethylene terephthalate. It is possible by making it thin with 100 microns in thickness to use tubed [like drawing 1] finally. Or as thickness was 500 microns and it was shown in drawing 4, the feed port 4 was formed on it, and the lateral portion was pasted together to the substrate for the lid 11 by the glue line 12. Saliva induction was made to carry out spreading desiccation of the lecithin which is a surface-active agent (8). When introducing saliva, the vent 10 penetrated in order to make it escape from air was formed in the substrate top or the lid 11. When saliva was promptly supplied to the feed port 4 with lecithin and there was the vent 10, saliva has been smoothly introduced to the polar zone. Triolein acid polyoxyethylene sorbitan other than lecithin, such as a nonionic surfactant, etc. can be used. In order to insert into a mouth, what has high safety is good. Although silver can also be used, if carbon is used, an electrode material is inexpensive and can be produced. Reaction part area was able to be measured in 5microl and a small quantity as a quantity of saliva, when the interval between the polar zone and a lid was 0.3 mm by 4 mm squares. Although the secretion speed of saliva changed with people, the saliva of the initial complement has been extracted in about a maximum of 2 minutes.

[0008]As shown in drawing 5, in front of the saliva feed port 4, when the fiber layer 13 which consists of cottons was added, saliva could be collected by capillarity from the wide range at the time of saliva extraction, and since the duty which filters the viscous materials in saliva was also carried out further, the accuracy of measurement was able to be raised.

[0009]The holding fixture 14 in the sensor mouth which formed the slot 15 for a sensor set was shown in drawing 6. It is difficult for a sensor to fluctuate with the weight of the display 3 that it is hard to add since it is thin, to insert in the hypoglottis and to hold. Then, by adding

and lower sides with a minimum of 2 cm, it can act as measurement Sadamu Nakayasu and can hold. The set of the sensor to a sensor display is simply made rightly by establishing the slot 15 for a sensor set in the inside of the holding fixture 14 in the sensor mouth. As for the sensor, ********** wipes the holding fixture 14 in the sensor mouth in alcohol after measuring finish the whole measurement. Since the distance to the caruncula sublingualis is constant when using it individually, if the position of the upper anterior tooth is described on the holding fixture 14 in the sensor mouth, a sensor is fixable to the simply same place.
[0010]If voltage is applied to the measurement pole 6 and the counter electrode 7 which were produced and saliva invades, it is detectable that detected that resistance very between two fell and saliva introduced. After detecting saliva introduction, when current 5 seconds after impressing +0.7V pulse voltage by the circuit in the display 3 on the basis of a counter electrode was measured 60 seconds after counting reaction time, almost similarly reaction time could be set up and the good response of reproducibility was obtained. Since it is pain when it has added to the mouth, if it emits a sound and is made to tell a test subject the time of detecting introduction of saliva, or after reaction-time progress, it is not necessary to add forever. The current value acquired by impressing pulse voltage is converted into glucose concentration based on the measuring gland obtained with the glucose reference solution, and it displays on the display 3. Since eyes worsen in many cases, the display of sugar concentration cannot read easily the person suffered from diabetes mellitus. Then, if the sugar concentration calculated by the display 3 is transmitted with a sound, it will become apparatus which is very easy to use. When the sugar concentration and the blood sugar level of saliva which were obtained were compared, the concentration in saliva correlated by about 0.01 time in blood, and flattery of change was also good. This showed that the sugar concentration measurement in saliva was effective.
[0011]The above-mentioned sensor can be used for the system in which redox enzyme, such as not only glucose but an alcohol sensor and a cholesterol sensor, participates. Alcohol oxidase, cholesterol oxidase, multienzyme, etc. can be used besides glucose oxidase as redox enzyme. An enzyme can also be fixed and used by a cross linking agent. In order that potassium ferricyanide may stabilize and react as an electron acceptor, it is suitable, but since reaction velocity is quick if p-benzoquinone is used, improvement in the speed is possible. 2,2-dichlorophenolindophenol, methylene blue, a phenazine methosulfate, beta-naphthoquinone 4-potassium sulfonate, etc. can be used.
[0012](Embodiment 2) Although the system which detects an enzyme reaction electrochemically was used in Embodiment 1, the method of detecting optically can also be used. Glucose is shown for the process of a reaction as one example. As shown in drawing 7, the reaction layer 17 and the fiber layer 13 have laminated on the transparent substrate 16. The reaction layer 17 impregnates and forms glucose oxidase, peroxidase, and an alt.toluidine in cellulose. Glucono lactone and hydrogen peroxide generate by glucose and glucose oxidase in saliva. The hydrogen peroxide generated by the catalysis of peroxidase oxidizes, and carries out coloration of the alt.toluidine blue. It stops, even if light is inputted for the absorbance which carried out coloration from the lower part of the transparent substrate 16 with a spectrometry machine and it measures a reflected light, and sugar concentration is calculated from the absorbance. When the accuracy of measurement was measured using the glucose reference solution, linearity was acquired from 0.3 mg/dl to 30 mg/dl. Since saliva does not contain many pigments like blood, it cannot block a color reaction but can measure it with sufficient accuracy.
[0013](Embodiment 3) Glucose in the saliva which requires sensitivity 100 times from blood sugar can be measured by considering it as the method of measuring a small amount of

layer 17 impregnates and forms glucose oxidase, peroxidase, and homovanillic acid in cellulose. Glucono lactone and hydrogen peroxide generate by glucose and glucose oxidase in saliva. The hydrogen peroxide generated by the catalysis of peroxidase oxidizes, and changes homovanillic acid into a fluorescent substance. The Measurement Division corresponding to a little glucose concentration called 0.02 mg/dl was possible by measuring this with a fluorophotometer (excited-wavelengths fluorescence wavelength of 425 nm of 315 nm). Even if it uses p-hydroxyphenylacetic acid instead of homovanillic acid, it is convertible for a fluorescent substance.

[0014]

[Effect of the Invention]By producing the biosensor for saliva which consists of a detection part which measures the saliva reaction part and reaction which consist of saliva induction, the electrode system which consists of a measurement pole and a counter electrode at least, an enzyme, and an electron acceptor in this invention, and measuring the sugar concentration in saliva, The sugar concentration simply correlated with the blood sugar level for a short time by aponia can be measured. In the system of reaction, not only an electrode method but an optical measurement method can be used. Not only sugar concentration but a specific component, for example, lactic acid, alcohol, etc. can be measured only by changing an enzyme system.

[Translation done.]

DESCRIPTION OF DRAWINGS

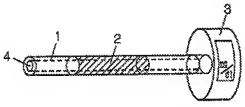
[Brief Description of the Drawings]
[Drawing 1]The figure showing the outline composition of the biosensor for saliva
[Drawing 2]The figure showing the outline composition of the biosensor for saliva
[Drawing 3]The figure showing the outline composition of the biosensor for saliva
[Drawing 4]The figure showing the outline composition of the biosensor for saliva
[Drawing 5]The figure showing the outline composition of the biosensor for saliva
[Drawing 6]The figure showing the outline composition of the biosensor for saliva
[Drawing 7]The figure showing the outline composition of the biosensor for saliva
[Explanations of letters or numerals]
1 Saliva induction
2 Reaction part
3 Display
4 Feed port
5 Substrate
6 Measurement pole
7 Counter electrode
8 Surface-active agent layer
9 and 17 Reaction layer
10 Vent
11 Lid
12 Glue line
13 Fiber layer
14 The holding fixture in the sensor mouth
15 The slot for a sensor set
16 Substrate

[Translation done.]

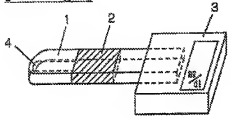
DRAWINGS

[Drawing 1]

1 試液導入部
2 反応部
3 表示部
4 導入口

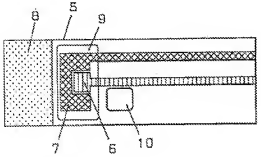


[Drawing 2]



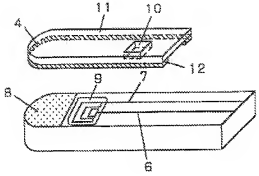
[Drawing 3]

5 基板
6 測定極
7 対極
8 界面活性剤層
9 反応層
10 空気孔



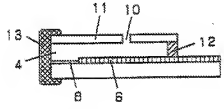
[Drawing 4]

11 フタ
12 接着層



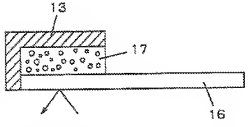
[Drawing 5]

13 繊維層



[Drawing 7]

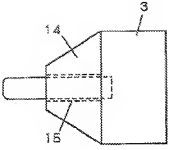
15 基板
17 反応層



[Drawing 6]

14 センサ口腔内保持具
15 センサセット用溝

(a)



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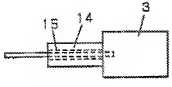

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